Patent Docket P0978-1C1D1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Avi J. Ashkenazi Serial No.: To be assigned Filed: August 21, 2001 For: Apo-2 Ligand	Group Art Unit: To be assigned Examiner: To be assigned

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

This Preliminary Amendment is being filed concurrently with Applicant's Rule 53(b) Divisional Application. Applicant respectfully requests entry of the following preliminary amendment prior to examination on the merits.

In the Specification:

Please delete pages 68-75 of the specification's originally filed Sequence Listing and enter into the specification the substitute Sequence Listing attached hereto (comprising page numbers 1-11).

On page 1, under the Title of the Invention, please insert the following paragraph:

RELATED APPLICATIONS

This application is a divisional application of US application serial no. 09/459,808 filed December 13, 1999, now pending, which is a continuation application of US application

serial no. 08/584,031 filed January 9, 1996, issued as US Patent No. 6,030,945, the contents of which applications are incorporated herein by reference. ---

On page 6, in the paragraphs on lines 19-24, the text has been amended to read:

-- Figure 1A shows the nucleotide sequence of human Apo-2 ligand cDNA (SEQ ID NO:2) and its derived amino acid sequence (SEQ ID NO:1).

Figure 1B shows an alignment of the C-terminal region of human Apo-2 ligand (Apo2L amino acids 114-281 of SEQ ID NO:1) with the corresponding region of known members of the human TNF cytokine family, 4-1BBL (SEQ ID NO:9), OX40L (SEQ ID NO:10), CD27L (SEQ ID NO:11), CD30L (SEQ ID NO:12), TNF-alpha (SEQ ID NO:13), LT-beta (SEQ ID NO:14), LT-alpha (SEQ ID NO:15), CD40L (SEQ ID NO:16), and Apo-1L (SEQ ID NO:17). ---

On pages 40-41, in the paragraph on lines 30-35 and 1-6, the text has been amended to read:

-- Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63]. ---

On pages 49-50, in the paragraph on lines 31-35 and 1-3, the text has been amended to read:

-- All restriction enzymes referred to in the examples were purchased from New England Biolabs and used according to manufacturer's instructions. All other commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas, Virginia. ---

On page 66, in the paragraph on lines 3-5, the text has been amended to read:

-- The following cell line has been deposited with the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia, USA (ATCC): ---

In the Claims:

Please cancel without prejudice claims 1-23, 25, 26, 28, and 29.

24. (As filed) A method of treating a mammal having cancer, comprising administering to a mammal diagnosed as having cancer an effective amount of Apo-2 ligand.

27. (As filed) The method of claim 24 wherein said cancer is breast cancer, prostate cancer or ovarian cancer.

Please add the following claims:

---30. A method of treating a mammal having prostate cancer, comprising administering to the mammal Apo-2 ligand polypeptide in an amount effective to induce cell death in the mammal's prostate cancer cells, wherein said Apo-2 ligand polypeptide is selected from the group consisting of:

(a) a polypeptide comprising amino acid residues 114-281 of Figure 1A (SEQ ID NO:1);

(b) a polypeptide consisting of amino acid residues 114-281 of Figure 1A (SEQ ID NO:1);

(c) a polypeptide consisting of amino acid residues 1-281 of Figure 1A (SEQ ID NO:1);

(d) a polypeptide which is a fragment of (a), (b) or (c).

31. The method of claim 30 wherein said Apo-2 ligand polypeptide consists of amino acid residues 114-281 of Figure 1A (SEQ ID NO:1).

32. The method of claim 30 or 31 wherein radiation therapy or chemotherapy is also administered to the mammal.

33. The method of claim 32 wherein the Apo-2 ligand polypeptide and the chemotherapy are administered concurrently.

34. The method of claim 32 wherein the Apo-2 ligand polypeptide and the chemotherapy are administered sequentially.

35. The method of claim 32 wherein the chemotherapy is selected from the group consisting of Doxorubicin, 5-Fluorouracil, Cytosine arabinoside, Cyclophosphamide, Thiotepa, Busulfan, Cytoxin, Taxol, Methotrexate, Cisplatin, Melphalan, Vinblastine, and Carboplatin.

36. The method of claim 30 or 31 wherein said Apo-2 ligand polypeptide is linked to one or more nonproteinaceous polymers selected from the group consisting of polyethylene glycol, polypropylene glycol, and polyoxyalkylene.

37. The method of claim 30 or 31 wherein said Apo-2 ligand polypeptide is unglycosylated.

38. The method of claim 37 wherein said Apo-2 ligand polypeptide is produced in *E. coli*. ---

REMARKS

Claims 1-23, 25, 26, 28, and 29, as originally filed in the parent application, have been canceled without prejudice. The present claims are provided in view of the Restriction Requirement entered in Applicant's prior application serial no. 09/459,808. Claims 30-38 have been added. Added claims 30-38 are fully supported by the specification on at least pages 6, 12, 24, 31, 33, 36, and 37, and accordingly, do not introduce new matter.

As shown above, certain amendments to the specification have been requested. In particular, the specification has been amended to reflect the current address of the ATCC depository. Further, Applicant is submitting herewith a paper copy of a substitute Sequence Listing which includes the sequences disclosed in Figure 1B. The specification has been amended to recite the appropriate sequence identifiers in the specification. It is believed that the substitute Sequence Listing brings the application into compliance with the rules provided in Sections 1.821-1.825.

The amendments to the specification and claims are illustrated in the attached pages entitled "Marked Up Version to Show Changes Made". For the Examiner's convenience, a clean copy of the now pending claims 24, 27, and 30-38 is provided above.

Respectfully submitted,
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MARKED UP VERSION TO SHOW CHANGES MADE

IN THE SPECIFICATION:

On page 1, under the Title of the Invention, the following paragraph has been inserted:

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On page 66, in the paragraph on lines 3-5, the text has been amended as follows:

-- The following cell line has been deposited with the American Type Culture Collection, [12301 Parklawn Drive, Rockville, MD] 10801 University Boulevard, Manassas, Virginia, USA (ATCC): ---

IN THE CLAIMS:

Claims 1-23, 25, 26, 28, and 29 have been canceled without prejudice.

The following claims 30-38 have been added:

---30. A method of treating a mammal having prostate cancer, comprising administering to the mammal Apo-2 ligand polypeptide in an amount effective to induce cell death in the mammal's prostate cancer cells, wherein said Apo-2 ligand polypeptide is selected from the group consisting of:

(a) a polypeptide comprising amino acid residues 114-281 of Figure 1A (SEQ ID NO:1);

(b) a polypeptide consisting of amino acid residues 114-281 of Figure 1A (SEQ ID NO:1);

(c) a polypeptide consisting of amino acid residues 1-281 of Figure 1A (SEQ ID NO:1);

(d) a polypeptide which is a fragment of (a), (b) or (c).

31. The method of claim 30 wherein said Apo-2 ligand polypeptide consists of amino acid residues 114-281 of Figure 1A (SEQ ID NO:1).

32. The method of claim 30 or 31 wherein radiation therapy or chemotherapy is also administered to the mammal.

33. The method of claim 32 wherein the Apo-2 ligand polypeptide and the chemotherapy are administered concurrently.

34. The method of claim 32 wherein the Apo-2 ligand polypeptide and the chemotherapy are administered sequentially.

35. The method of claim 32 wherein the chemotherapy is selected from the group consisting of Doxorubicin, 5-Fluorouracil, Cytosine arabinoside, Cyclophosphamide, Thiotepa, Busulfan, Cytoxin, Taxol, Methotrexate, Cisplatin, Melphalan, Vinblastine, and Carboplatin.

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